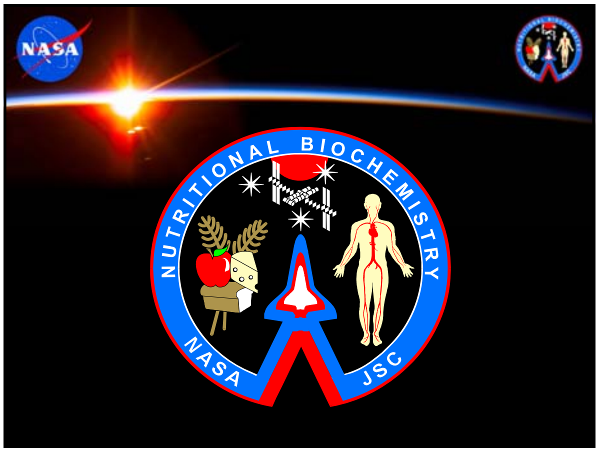
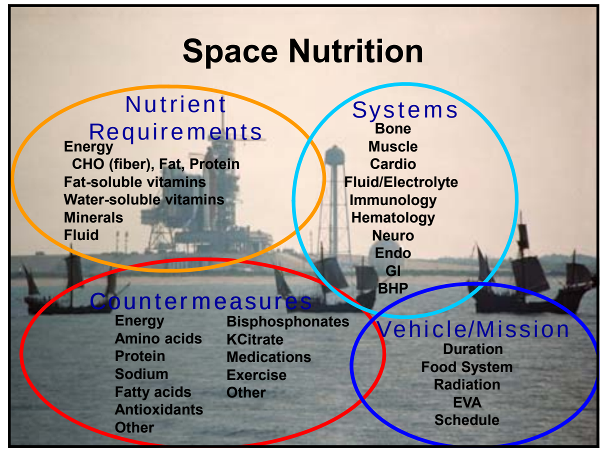
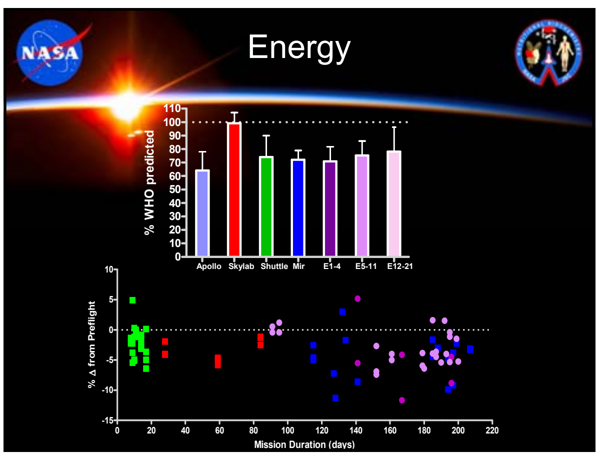
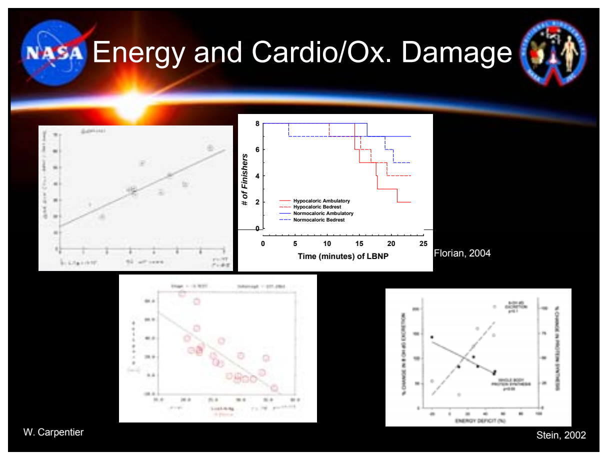
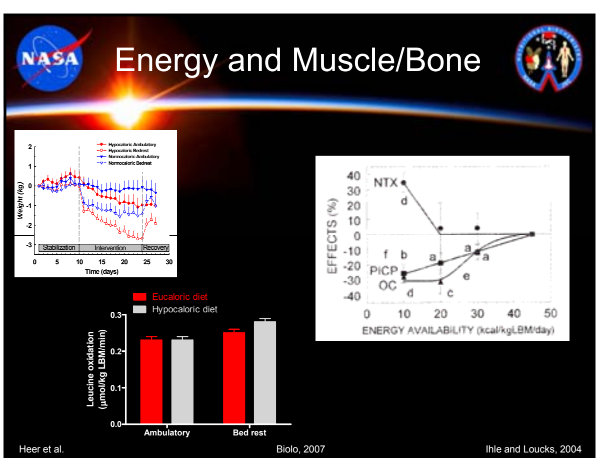
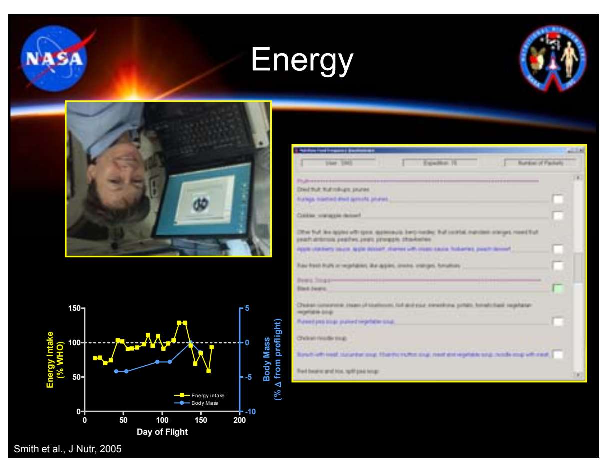

NASA
NUTRITIONAL BIOCHEMISTRY
NASA JSC

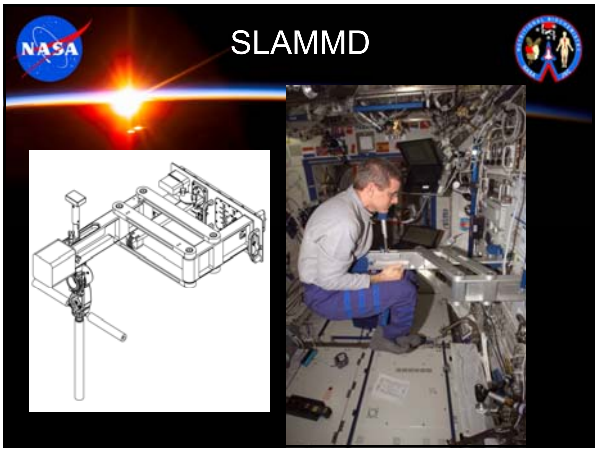

Space Nutrition
Nutrient Requirements
Energy
CHO (fiber), Fat, Protein
Fat-soluble vitamins
Water-soluble vitamins
Minerals
Fluid
Systems
Bone
Muscle
Cardio
Fluid/Electrolyte
Immunology
Hematology
Neuro
Endo
GI
BHP
Countermeasures
Energy
Amino acids
Protein
Sodium
Fatty acids
Antioxidants
Other
Bisphosphonates
KCitrate
Medications
Exercise
Other
Vehicle/Mission
Duration
Food System
Radiation
EVA
Schedule


NASA
Energy
% WHO predicted
Apollo
Skylab
Shuttle
Mir
E1-4
E5-11
E12-21
% Δ from Preflight
Mission Duration (days)


NASA
Energy and Cardio/Ox. Damage
# of Finishers
Hypocaloric Ambulatory
Hypocaloric Bedrest
Normocaloric Ambulatory
Normocaloric Bedrest
Time (minutes) of LBNP
Florian, 2004
W. Carpentier
Stein, 2002

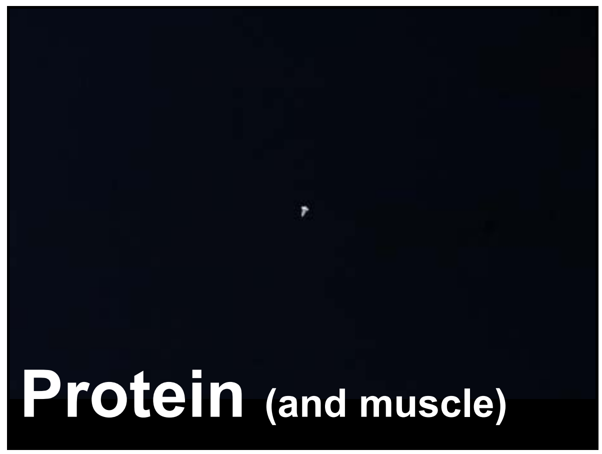

NASA
Energy and Muscle/Bone
Hypocaloric Ambulatory
Hypocaloric Bedrest
Normocaloric Ambulatory
Normocaloric Bedrest
Weight (kg)
Stabilization
Intervention
Recovery
Time (days)
NTX
PICP
OC
EFFECTS (%)
ENERGY AVAILABILITY (kcal/kgLBM/day)
Eucaloric diet
Hypocaloric diet
Leucine oxidation (µmol/kg LBM/min)
Ambulatory
Bed rest
Heer et al.
Biolo, 2007
Ihle and Loucks, 2004

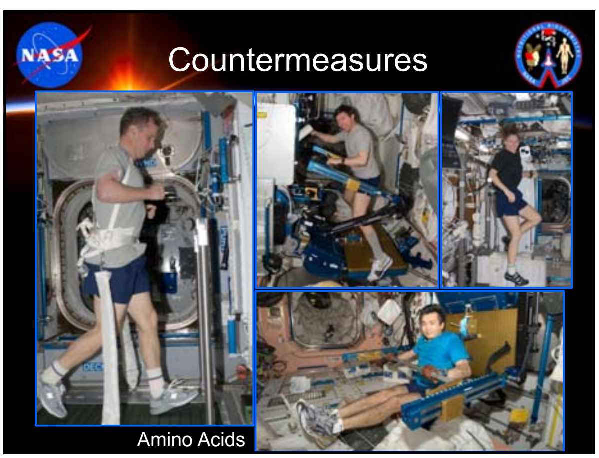

NASA
Energy
Energy Intake (% WHO)
Body Mass (% Δ from preflight)
Energy intake
Body Mass
Day of Flight
Smith et al., J Nutr, 2005

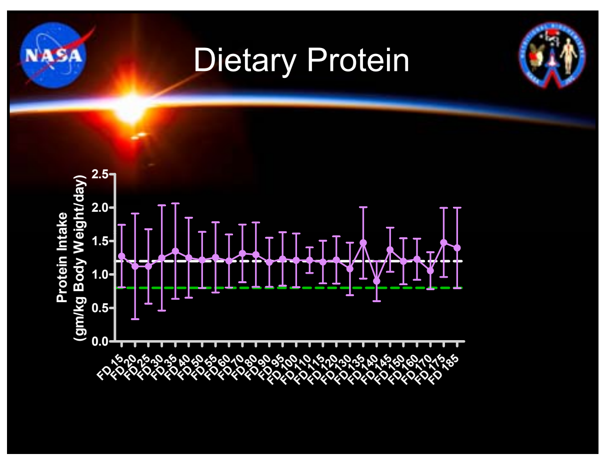

SLAMMD


Nutrition SMO


Nutrition SMO


Protein (and muscle)


Countermeasures
Amino Acids


Dietary Protein
Protein Intake
(gm/kg Body Weight/day)
2.5
2.0
1.5
1.0
0.5
0.0
FD 15
FD 20
FD 25
FD 30
FD 35
FD 40
FD 50
FD 55
FD 60
FD 70
FD 80
FD 90
FD 95
FD 100
FD 110
FD 115
FD 120
FD 130
FD 135
FD 140
FD 145
FD 150
FD 160
FD 170
FD 175
FD 185

Muscle Protein

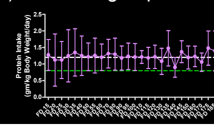
↓ Protein Synthesis ↑ Protein Breakdown

Amino Acids

Amino acid supplementation

Issues:

- Protein synthesis vs. breakdown
- Exercise
- Catabolic effectors (e.g., stress/cortisol, hypocaloric diet, T3)
- Intake (and/or supplement) of control group



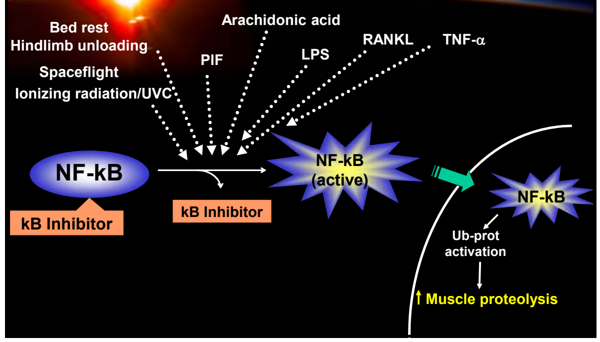
Protein Synthesis Breakdown

Unloading-induced atrophy is a relatively uncomplicated form of muscle loss…. most of the loss of muscle mass during disuse atrophy can be accounted for by a depression in the rate of protein synthesis.

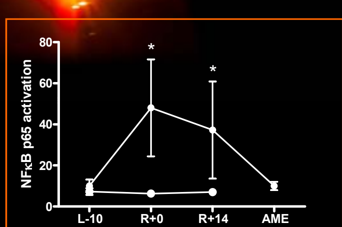
whereas in disease states associated with inflammation (cancer cachexia, AIDS, burns, sepsis, and uremia), there is a *procatabolic hormonal and cytokine environment*. ….

Phillips, et al, J Appl Physiol, 2009

Inflammation

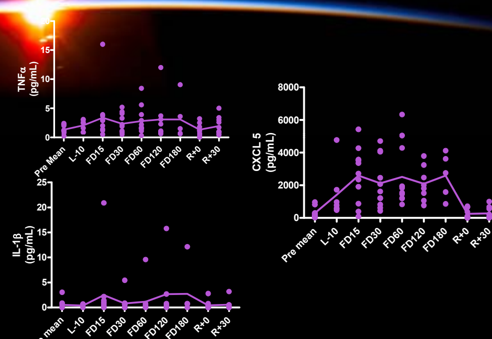


…procatabolic hormonal and cytokine environment…

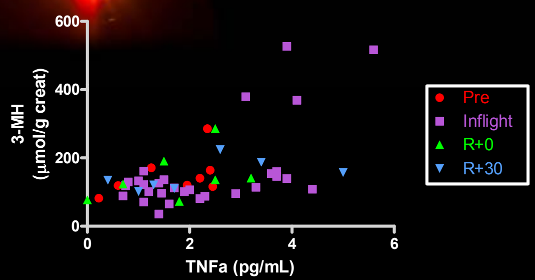


Pierson et al., 2009

Inflammatory Markers



Inflammation/Muscle



Protein/Muscle

It is imperative that these studies include examination of dynamic measures of muscle protein turnover and putative metabolic controllers… ***unless we have a clear idea of the basic responses to immobilization*** per se, the effects of such factors will not be easily teased out and ***therapeutic goals will remain largely unattainable.***

Phillips, et al, J Appl Physiol, 2009

Hypercatabolism

Hyper-catabolic conditions associated with proteolysis:

- Cancer cachexia
- Cachexia associated with heart failure
- Sepsis
- Starvation
- Metabolic acidosis
- Stress/trauma associated with excess glucocorticoids
- Space flight

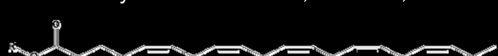
Hypercatabolism

Hyper-catabolic conditions associated with upregulation of the ubiquitin-proteasome system:

- Cancer cachexia (Lorite et al. 2001; Tisdale et al. 2009)
- Cachexia associated with heart failure (Filippatos et al. 2005, Freeman et al. 1998)
- Sepsis (Voisin et al. 1996; Tiao et al. 1994)
- Starvation (Whitehouse, 2001)
- Metabolic acidosis (Mitch et al. 1994)
- Stress/trauma associated with excess glucocorticoids (Wing et al. 1993; Biolo et al. 2000)
- Space flight (Ikemoto et al. 2001; Riley et al. 1992)

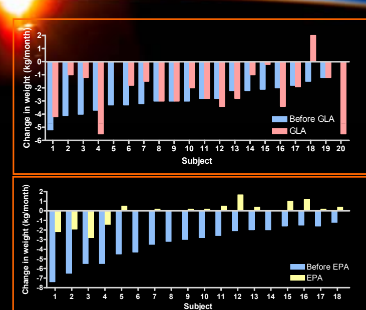
Omega 3 (n3) Fatty Acids

- Eicosapentaenoic acid (EPA)
  - 20-C, omega-3 fatty acid
  - Dietary sources: fish oil, flaxseed, walnuts



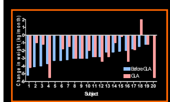
  - Beneficial effects on cholesterol, lipid metabolism, and cardiovascular health

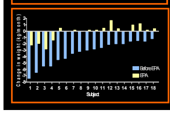
n3/EPA and Muscle

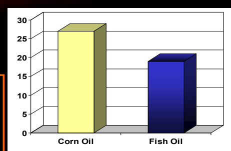


Whitehouse et al. 2001

Omega-3 and Cancer







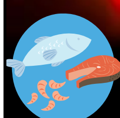
Proportion of tumor bearing rats

Vanamala et al., Carcinogenesis, 2008

Vitamin D

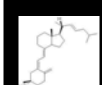
Vitamin D

Sources



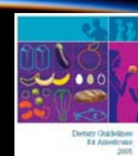
- UVB radiation
- Food
  - Seafood, mushrooms, egg yolk,
  - Fortified foods

Nomenclature



- Vitamin D_2 (ergocalciferol)
- Vitamin D_3 (cholecalciferol)
- 25-OH vitamin D
- 1,25 $(OH)_2$ vitamin D

Vitamin D Intake Guidelines



RDA (1997 IOM)

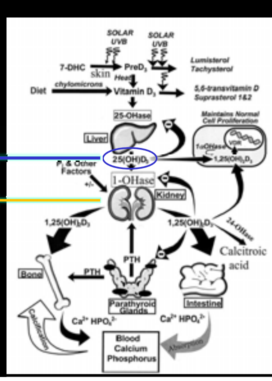
- 19-50 y: 200 IU/d
- 50-70 y: 400 IU/d

The 2005 Dietary Guidelines for Americans recommendation advised older adults, people with dark skin, and people exposed to insufficient sunlight to consume 1000 IU/d.

Vitamin D

Vitamin D Status

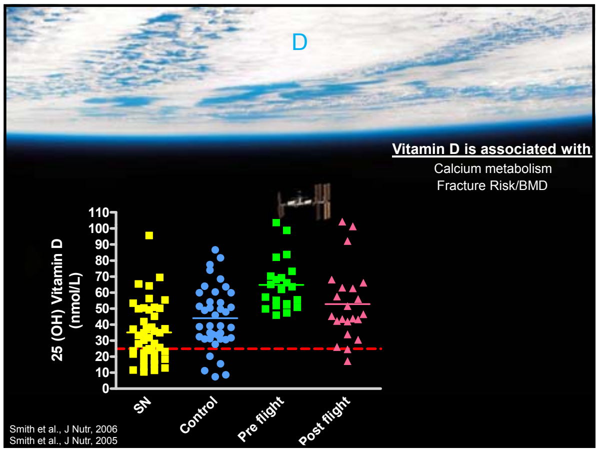
Other metabolites:
$24,25(OH)_2D_3$
$25,26(OH)_2D_3$
35 others…

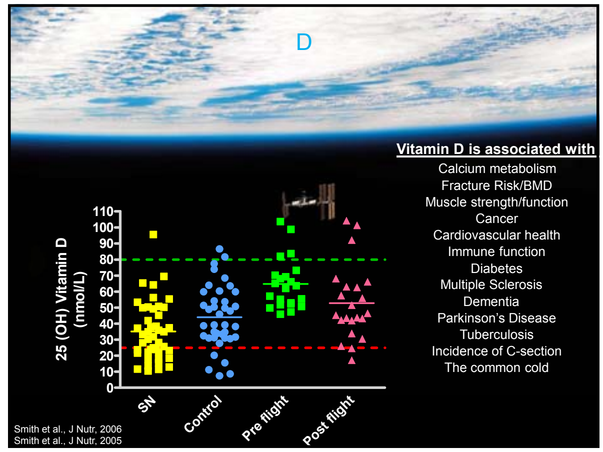


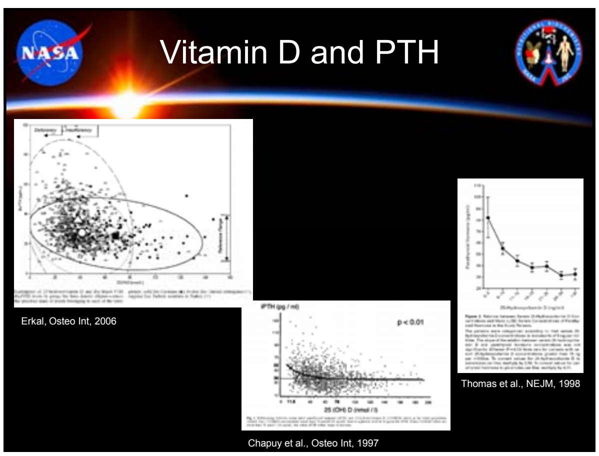
Holick, AJCN, 2004

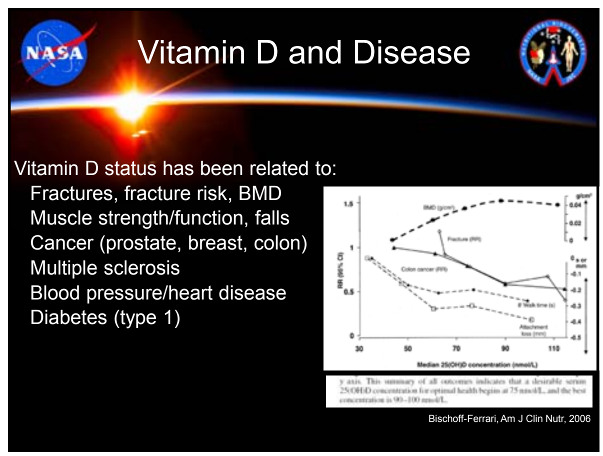
Contributing Factors to Vitamin D Status

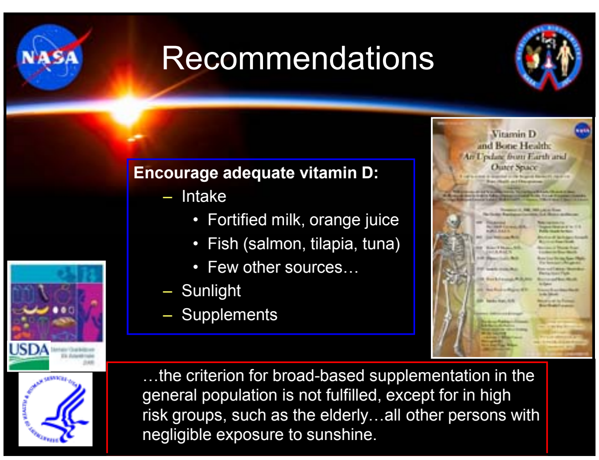
- Age
- Ethnicity
- Salt-sensitive hypertension
  - Increased protein excretion in salt-sensitive individuals and Dahl rats with salt loading
- Adiposity/obesity

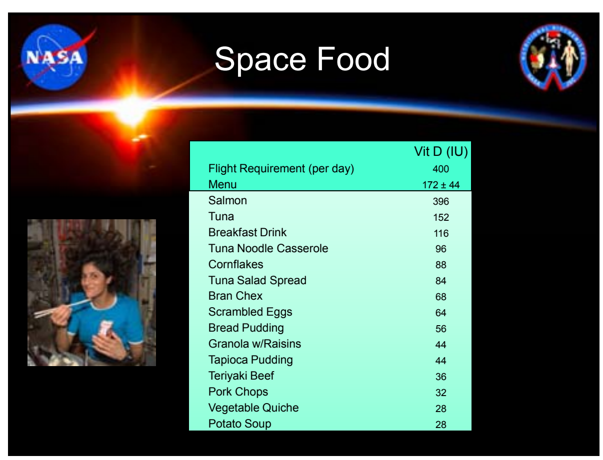












	Vit D (IU)
Flight Requirement (per day)	400
Menu	172 ± 44
Salmon	396
Tuna	152
Breakfast Drink	116
Tuna Noodle Casserole	96
Cornflakes	88
Tuna Salad Spread	84
Bran Chex	68
Scrambled Eggs	64
Bread Pudding	56
Granola w/Raisins	44
Tapioca Pudding	44
Teriyaki Beef	36
Pork Chops	32
Vegetable Quiche	28
Potato Soup	28

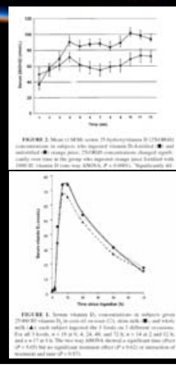
Upper Limits

- 2000 IU/day is current defined IOM no observed adverse events limit (NOAEL)
- Studies of higher levels have proven safe…

> We present a risk assessment based on relevant, well-designed human clinical trials of vitamin D. Collectively, the absence of toxicity in trials conducted in healthy adults that used vitamin D dose ≥250 μg/d (10 000 IU vitamin D_3) supports the confident selection of this value as the UL. *Am J Clin Nutr* 2007;85:6–18.

Hathcock et al., AJCN, 2007

- Sunlight does not result in toxicity
- Watch multivitamins (vit A and other nutrients may be in excess)



Vitamin D Toxicity

Hypercalcemia, hypercalciuria, soft tissue calcification, kidney stones

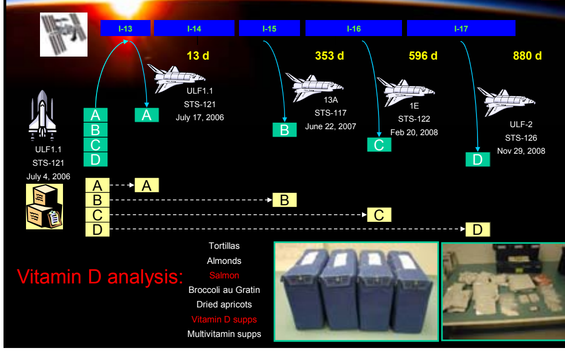
Vitamin D

Vitamin D status goes down after long-duration spaceflight.

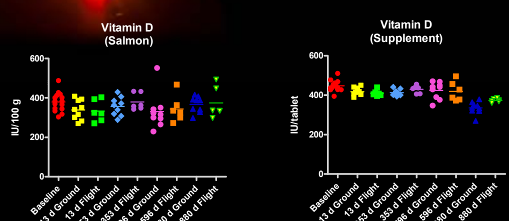
Questions:

- Is the stability of vitamin D in the food system and supplement different during spaceflight?
- Is the daily dose not high enough to maintain status?
- Does vitamin D metabolism change during spaceflight?

Stability Study



Stability Study



(Zwart et al., 2009)

Stability Study

Stability of vitamin D in food/supplement is not altered during spaceflight

Question:

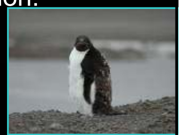
- Is the daily dose simply not high enough to maintain status in an environment with no sun exposure?

Polar Vitamin D

3 levels of vitamin D supplementation:
- 400 IU/d (n = 18)
- 1000 IU/d (n = 19)
- 2000 IU/d (n = 18)

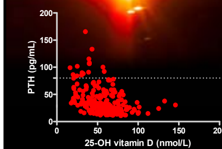
3 blood collections and diet logs
- 25D, 1,25D, PTH, Ca, VDBP, NTX

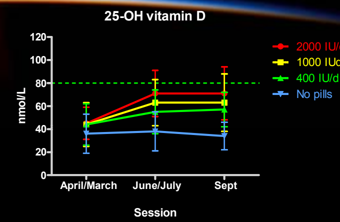
Double blinded supplementation

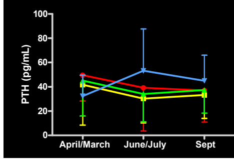


(Smith et al., 2009)

Polar Vitamin D







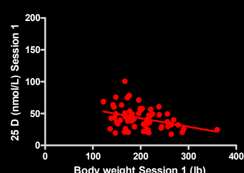
Compliance

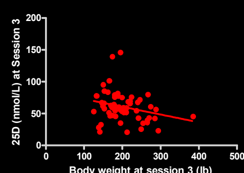
84% on average

(Smith et al., 2009)

Polar Vitamin D

Vitamin D status is related to body weight…
- what if we exclude subjects with BMI >29 kg/m²?

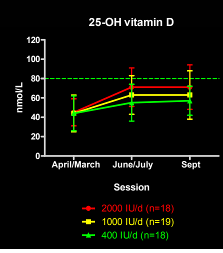


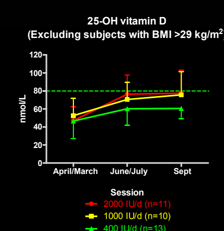


(Smith et al., 2009)

Polar Vitamin D

1000 or 2000 IU/d was enough to reach 80 nmol/L and maintain vitamin D status





Residual Questions…

Could compliance be improved with a weekly dose instead of a daily dose?

Is vitamin D status related to observed changes in immune function during polar winters?

Polar II

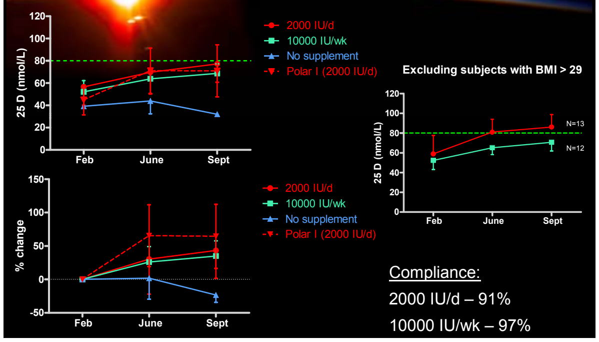
2,000 IU/d (n=15)

10,000 IU/wk (n=14)

Vitamin D, Calcium

Immune Markers

Polar II



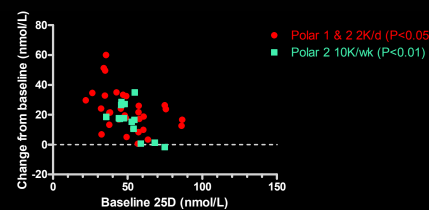
Compliance:

2000 IU/d – 91%

10000 IU/wk – 97%

Polar II

In addition to BMI, the efficacy of vitamin D supplementation is affected by baseline status

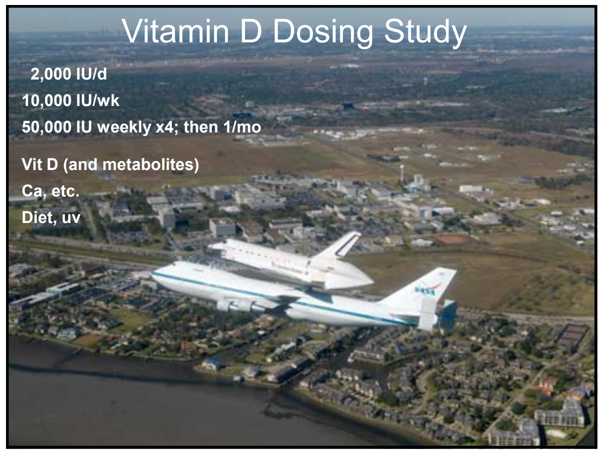


Residual Questions…

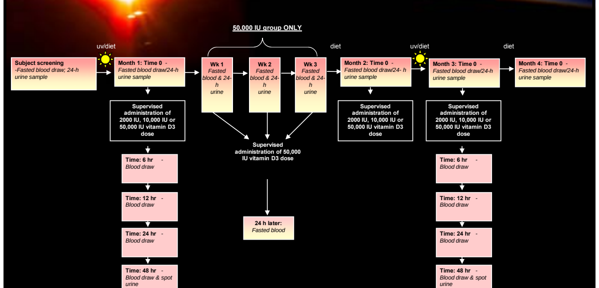
Is a higher, less frequent dose as effective as a daily or weekly dose?

Does a high dose result in a high serum concentration of 25-OH vitamin D (or metabolites) or alter serum or urine calcium?

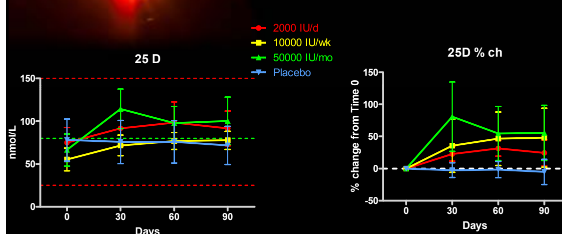
Vitamin D Dosing Study

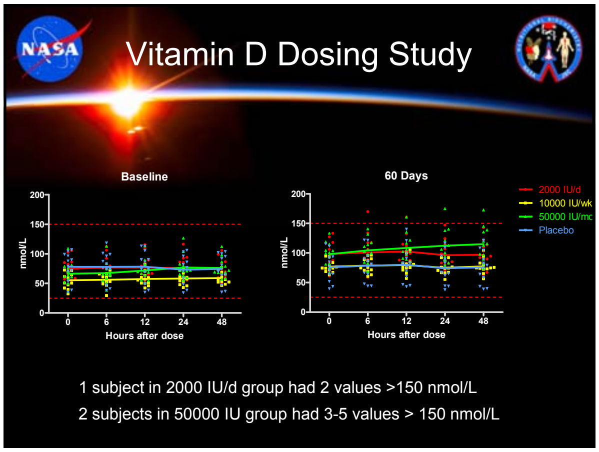


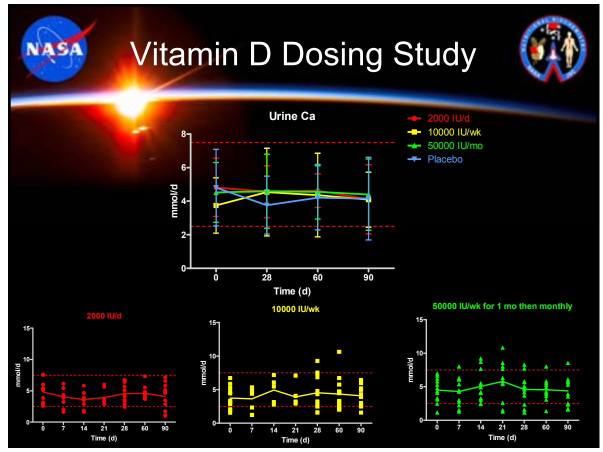
Vitamin D Dosing Study

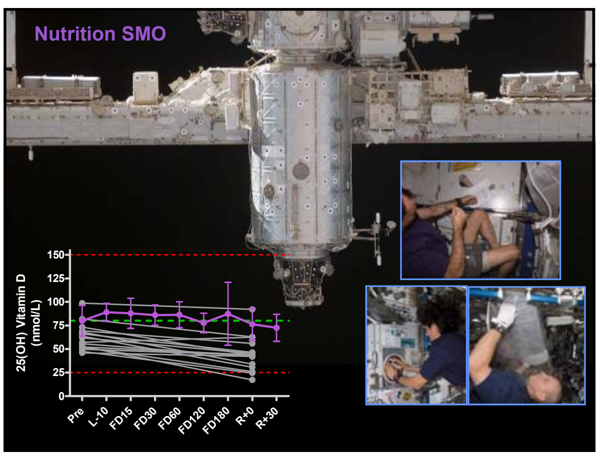


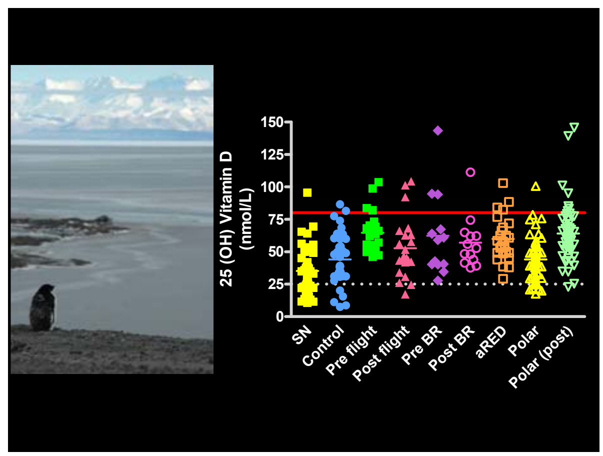
Vitamin D Dosing Study

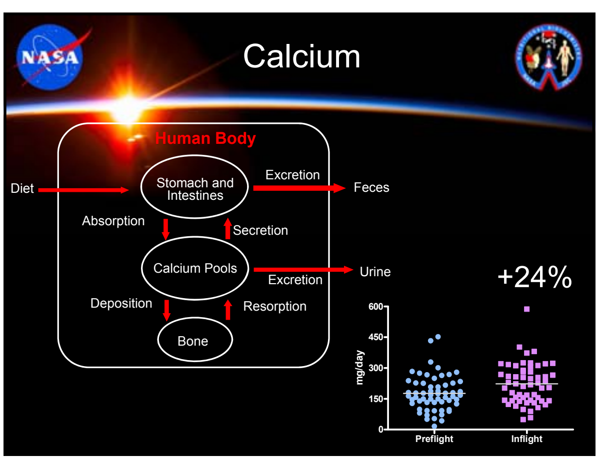


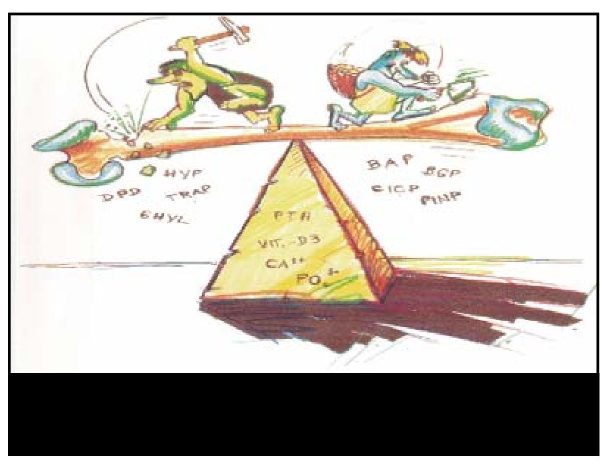

Vitamin D Dosing Study
Baseline
60 Days
nmol/L
Hours after dose
2000 IU/d
10000 IU/wk
50000 IU/mo
Placebo
1 subject in 2000 IU/d group had 2 values >150 nmol/L
2 subjects in 50000 IU group had 3-5 values > 150 nmol/L


Vitamin D Dosing Study
Urine Ca
2000 IU/d
10000 IU/wk
50000 IU/mo
Placebo
mmol/d
Time (d)
2000 IU/d
10000 IU/wk
50000 IU/wk for 1 mo then monthly

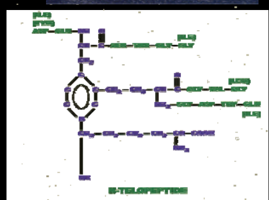

Nutrition SMO
25(OH) Vitamin D (nmol/L)
Pre
L-10
FD15
FD30
FD60
FD120
FD180
R+0
R+30

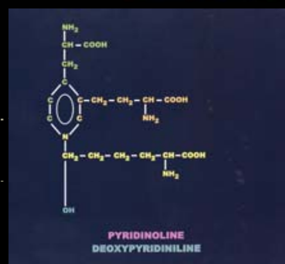

25 (OH) Vitamin D (nmol/L)
SN
Control
Pre flight
Post flight
Pre BR
Post BR
aRED
Polar
Polar (post)


Calcium
Human Body
Diet
Stomach and Intestines
Excretion
Feces
Absorption
Secretion
Calcium Pools
Excretion
Urine
Deposition
Resorption
Bone
+24%
mg/day
Preflight
Inflight



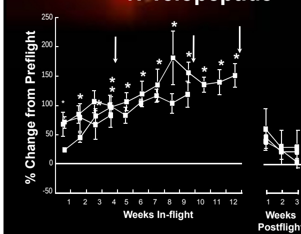
Collagen Crosslinks





Bone Resorption

N-Telopeptide



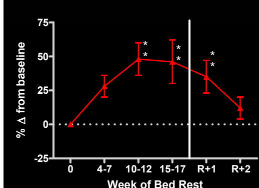
Space Flight:

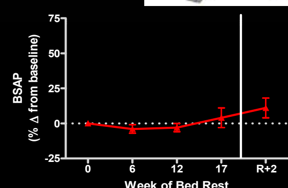
↑ Urinary collagen xlinks
↑ Urinary Ca
↑ Urinary OH-Proline
↑ V_{o-}

Bone resorption is increased during flight

Smith et al., JCEM, 1998

Bone Formation/Resorption





Calcium Isotopes

40Ca	42Ca	43Ca	44Ca	46Ca	48Ca
97%	0.65%	0.11%	2.09%	0.004%	0.19%

$$\delta^{44}Ca = \left(\frac{^{44}Ca/^{40}Ca_{sample}}{^{44}Ca/^{40}Ca_{standard}} - 1\right) \times 1000$$

Calcium Isotopes

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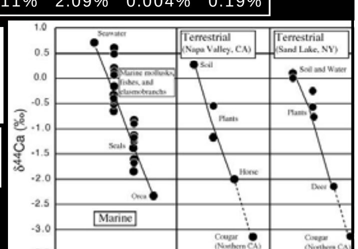
$$\delta^{44}Ca = \left(\frac{^{44}Ca/^{40}Ca_{sample}}{^{44}Ca/^{40}Ca_{standard}} - 1\right) \times 1000$$

Higher δ44Ca = "heavier"
Lower δ44Ca = "lighter"



Calcium Isotopes

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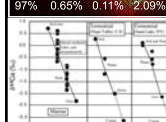

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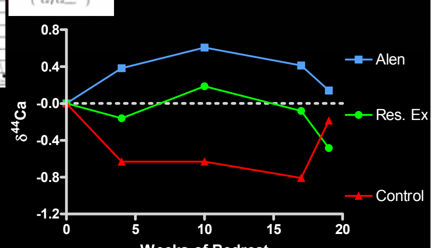
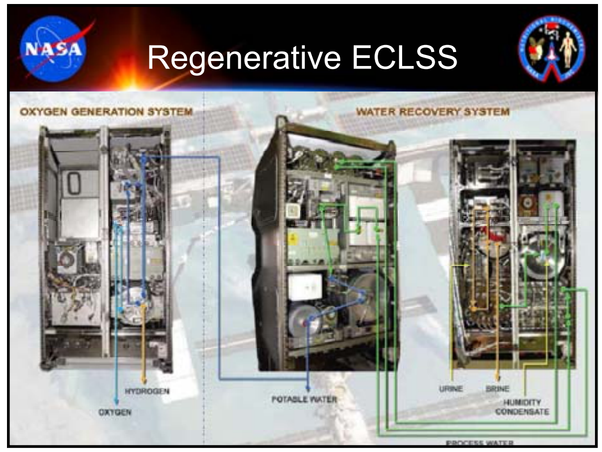
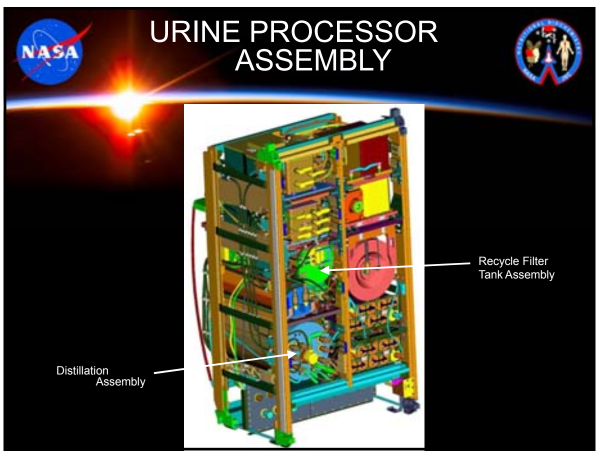


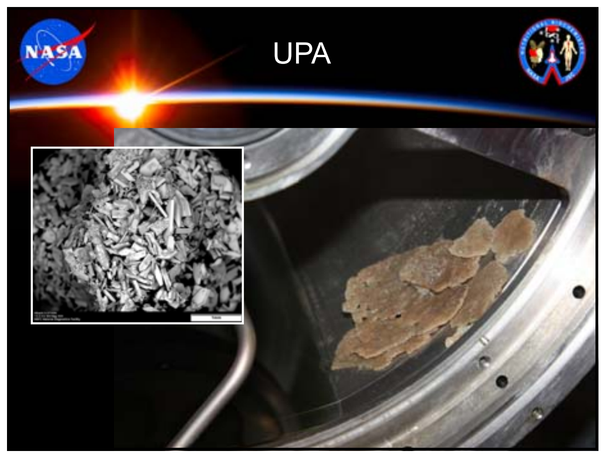
Skulan et al., Clin Chem, 2007



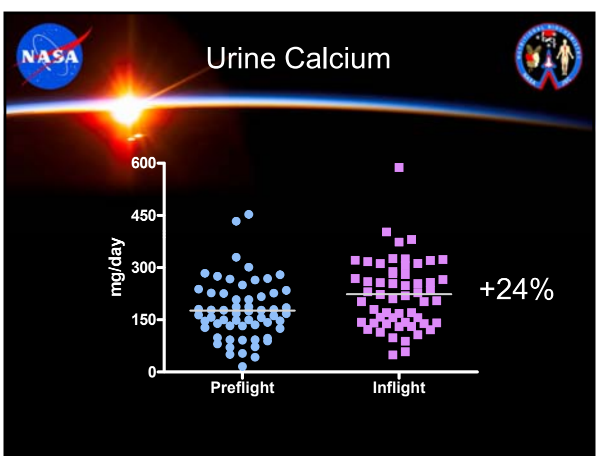
Regenerative ECLSS
OXYGEN GENERATION SYSTEM
WATER RECOVERY SYSTEM
HYDROGEN
OXYGEN
POTABLE WATER
URINE
BRINE
HUMIDITY CONDENSATE



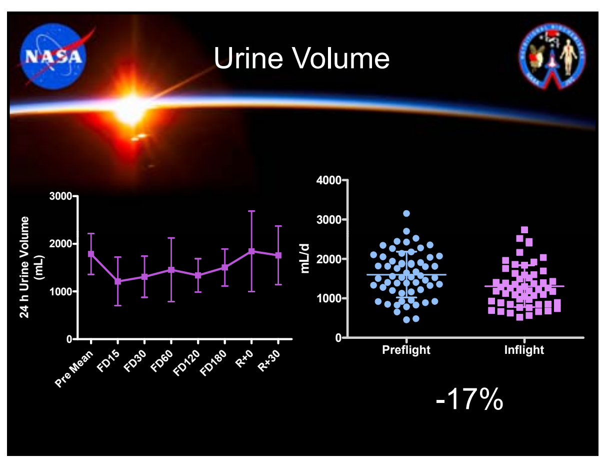
URINE PROCESSOR ASSEMBLY
Recycle Filter Tank Assembly
Distillation Assembly



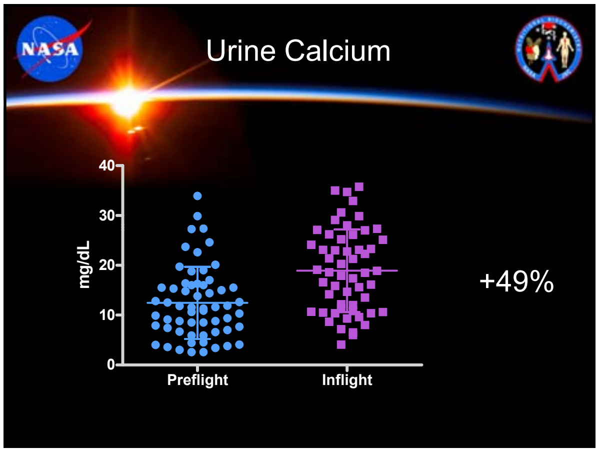
UPA

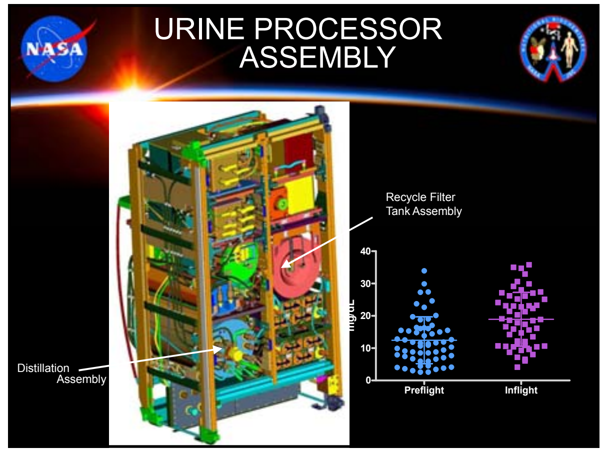


Urine Calcium
mg/day
600
450
300
150
0
Preflight
Inflight
+24%



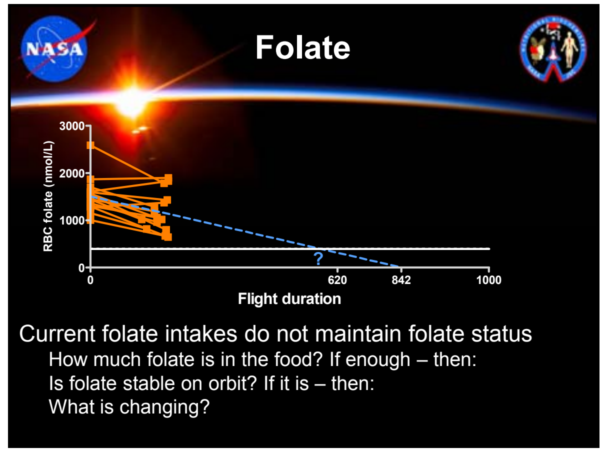
Urine Volume
24 h Urine Volume (mL)
3000
2000
1000
0
Pre Mean
FD15
FD30
FD60
FD120
FD180
R+0
R+30
mL/d
4000
3000
2000
1000
0
Preflight
Inflight
-17%


Urine Calcium
NASA
40
30
20
10
0
mg/dL
Preflight
Inflight
+49%

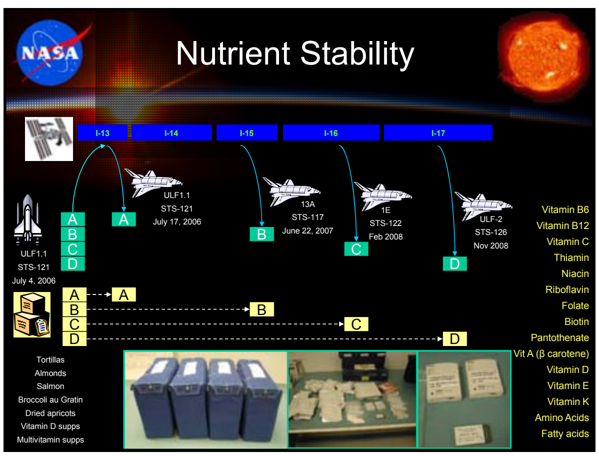

URINE PROCESSOR ASSEMBLY
NASA
Recycle Filter
Tank Assembly
Distillation
Assembly
mg/dL
Preflight
Inflight


Nutrition SMO
NASA

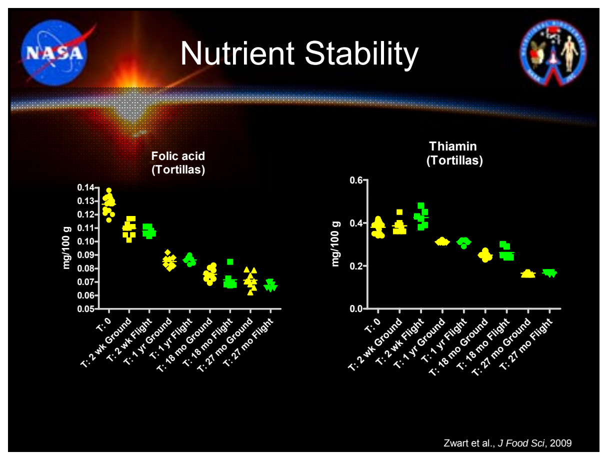

BLOOD (7ml SERUM)



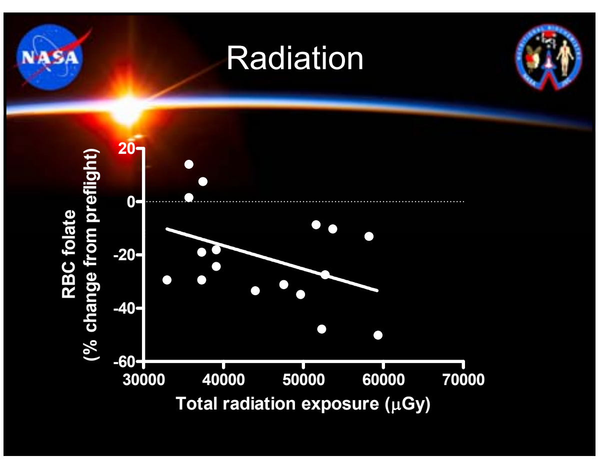
Folate
RBC folate (nmol/L)
3000
2000
1000
0
0
620
842
1000
?
Flight duration
Current folate intakes do not maintain folate status
How much folate is in the food? If enough – then:
Is folate stable on orbit? If it is – then:
What is changing?



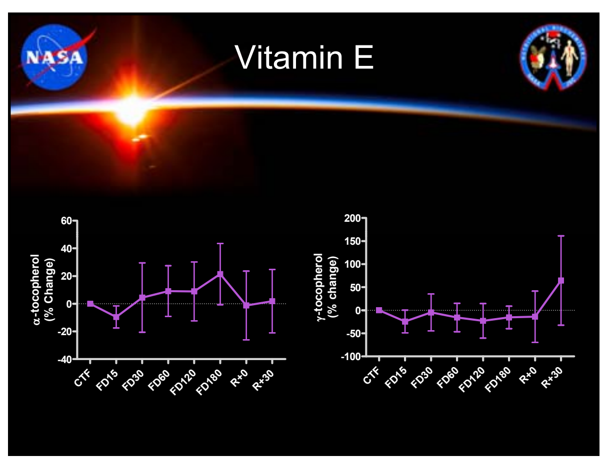
Nutrient Stability
I-13
I-14
I-15
I-16
I-17
ULF1.1
STS-121
July 17, 2006
13A
STS-117
June 22, 2007
1E
STS-122
Feb 2008
ULF-2
STS-126
Nov 2008
ULF1.1
STS-121
July 4, 2006
A
B
C
D
Tortillas
Almonds
Salmon
Broccoli au Gratin
Dried apricots
Vitamin D supps
Multivitamin supps
Vitamin B6
Vitamin B12
Vitamin C
Thiamin
Niacin
Riboflavin
Folate
Biotin
Pantothenate
Vit A (β carotene)
Vitamin D
Vitamin E
Vitamin K
Amino Acids
Fatty acids



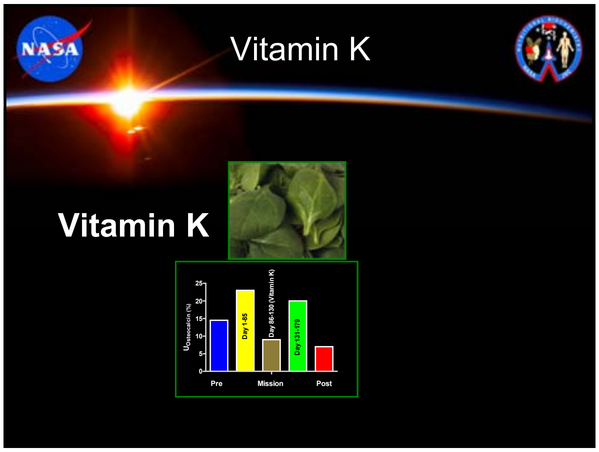
Nutrient Stability
Folic acid
(Tortillas)
mg/100 g
Thiamin
(Tortillas)
T: 0
T: 2 wk Ground
T: 2 wk Flight
T: 1 yr Ground
T: 1 yr Flight
T: 18 mo Ground
T: 18 mo Flight
T: 27 mo Ground
T: 27 mo Flight
Zwart et al., J Food Sci, 2009

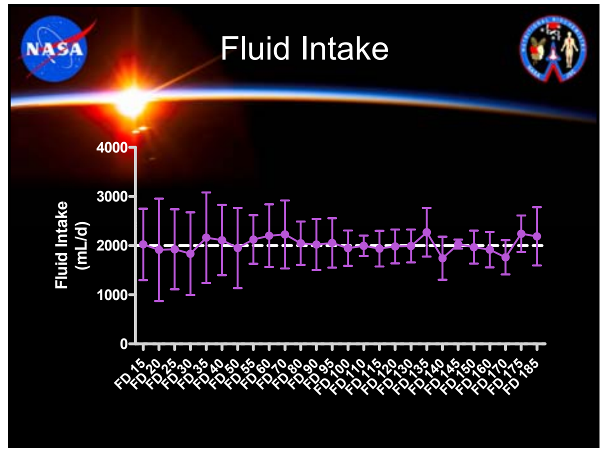


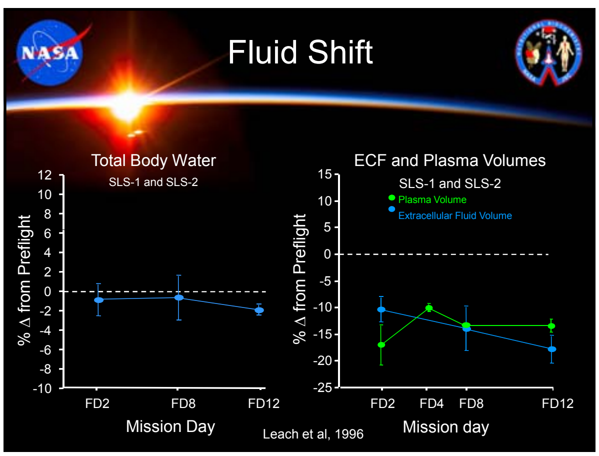
Radiation
RBC folate
(% change from preflight)
20
0
-20
-40
-60
30000
40000
50000
60000
70000
Total radiation exposure (μGy)

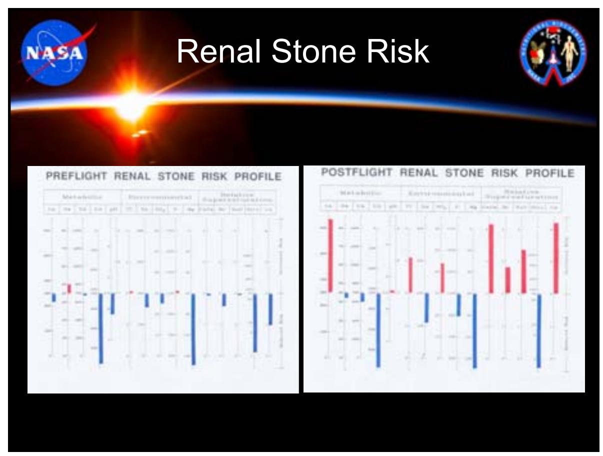


Vitamin E
α-tocopherol
(% Change)
γ-tocopherol
(% change)
CTF
FD15
FD30
FD60
FD120
FD180
R+0
R+30

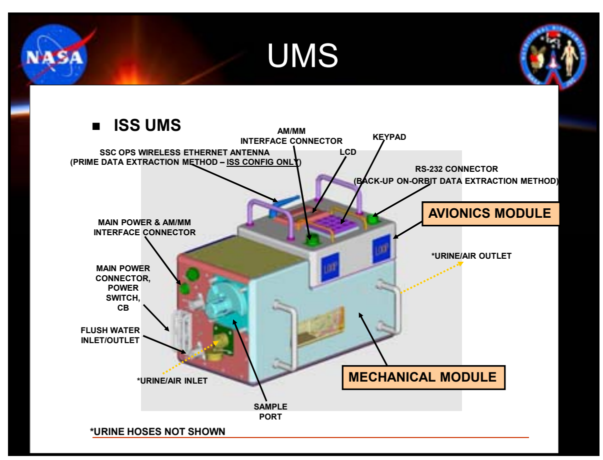

Vitamin K
Vitamin K
Pre
Mission
Post
Day 1-85
Day 86-130 (Vitamin K)
Day 131-179

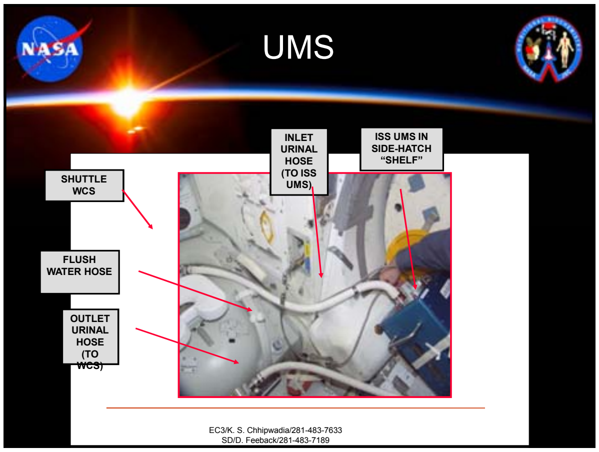

Fluid Intake
Fluid Intake (mL/d)
4000
3000
2000
1000
0
FD 15
FD 20
FD 25
FD 30
FD 35
FD 40
FD 50
FD 55
FD 60
FD 70
FD 80
FD 90
FD 95
FD 100
FD 110
FD 115
FD 120
FD 130
FD 135
FD 140
FD 145
FD 150
FD 160
FD 170
FD 175
FD 185


Fluid Shift
Total Body Water
SLS-1 and SLS-2
% Δ from Preflight
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
FD2
FD8
FD12
Mission Day
ECF and Plasma Volumes
SLS-1 and SLS-2
Plasma Volume
Extracellular Fluid Volume
% Δ from Preflight
15
10
5
0
-5
-10
-15
-20
-25
FD2
FD4
FD8
FD12
Mission day
Leach et al, 1996


Renal Stone Risk
PREFLIGHT RENAL STONE RISK PROFILE
POSTFLIGHT RENAL STONE RISK PROFILE


Nutrition SMO


UMS
ISS UMS
AM/MM INTERFACE CONNECTOR
KEYPAD
SSC OPS WIRELESS ETHERNET ANTENNA (PRIME DATA EXTRACTION METHOD – ISS CONFIG ONLY)
LCD
RS-232 CONNECTOR (BACK-UP ON-ORBIT DATA EXTRACTION METHOD)
AVIONICS MODULE
MAIN POWER & AM/MM INTERFACE CONNECTOR
*URINE/AIR OUTLET
MAIN POWER CONNECTOR, POWER SWITCH, CB
FLUSH WATER INLET/OUTLET
*URINE/AIR INLET
MECHANICAL MODULE
SAMPLE PORT
*URINE HOSES NOT SHOWN



Sodium

Nutritional Biochemistry Laboratory | SK/S.M. Smith | Feb 23, 2010

Excess sodium intake (and related effects on acid/base physiology) is associated with a number of health issues

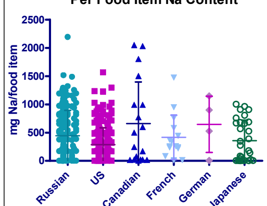
- Bone loss
- Increased renal stone risk
- Impaired muscle performance/protein catabolism
- Altered glucose metabolism
- Altered vitamin D metabolism
- Hypertension

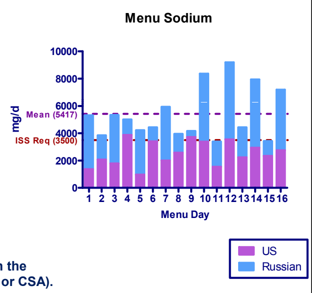
With the exception of hypertension, all of these other factors have been raised as concerns for space travelers.

Sodium

Nutritional Biochemistry Laboratory | SK/S.M. Smith | Feb 23, 2010

The space food system is very high in sodium



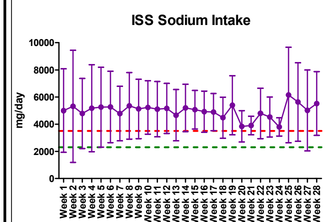


NOTE: only a few JAXA food items are on the standard menu at this point (and no ESA or CSA). These are included in the bonus foods per crew request (along with other non-standard foods)

Sodium

Nutritional Biochemistry Laboratory | SK/S.M. Smith | Feb 23, 2010

Sodium intake during flight is very high



3500 mg/d = ISS requirement (JSC-28038); and the "old" RDA)

2300 mg/d = US Dietary Reference Intake Tolerable Upper Intake Level (UL)**, and NASA exploration requirement (JSC-63555)

In 2005-2006, the average US intake of Na was estimated at 3,436 mg Na/d*

In 1990-1999, the average US intake of Na was estimated at: 3,377 mg for 31-50 yo M**

3,539 mg for 31-50 yo F

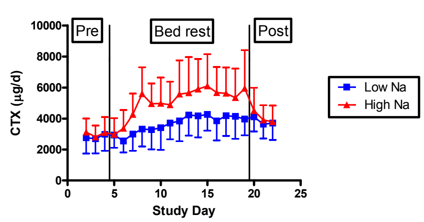
* http://www.cdc.gov/media/pressrel/2009/r090326.htm

** IOM, Dietary Reference Intakes, 2004

SOLO, etc.

Nutritional Biochemistry Laboratory | SK/S.M. Smith | Feb 23, 2010

High sodium has been shown in bed rest (and ambulatory) studies to exacerbate bone breakdown (Heer, et al.)



Low = 0.7 mEq Na/kg = 16.1 mg/kg; 1127 mg for 70 kg person

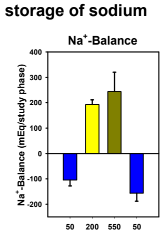
High = 7.7 mEq Na/kg = 177.1 mg/kg; 12397 mg for 70 kg person

NOTE: This is the basis for the ESA sponsored SOLO experiment on ISS.

Mechanism

Nutritional Biochemistry Laboratory | SK/S.M. Smith | Feb 23, 2010

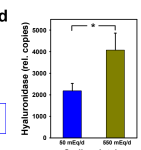
Excess sodium intake leads to non-osmotic (i.e., non-fluid retaining) storage of sodium

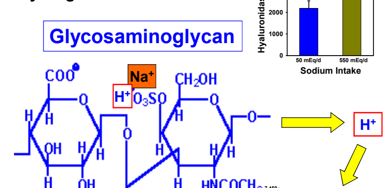


Heer, et al., *BJN*, 2009

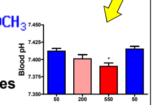
50 mEq = 1150 mg
200 mEq = 4600 mg
550 mEq = 12,650 mg

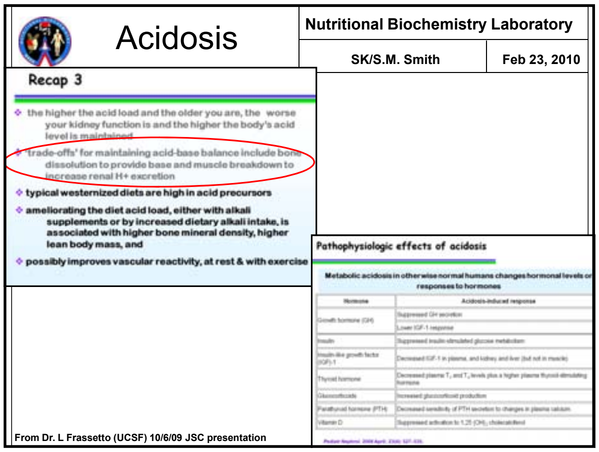
The excess sodium is bound to glycosaminoglycans in skin, exchanging with a hydrogen ion.

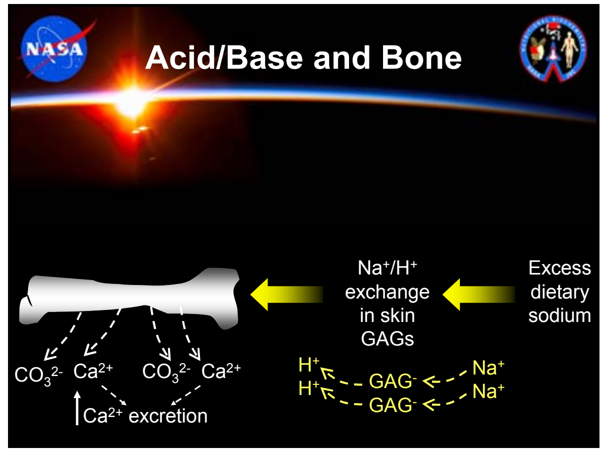




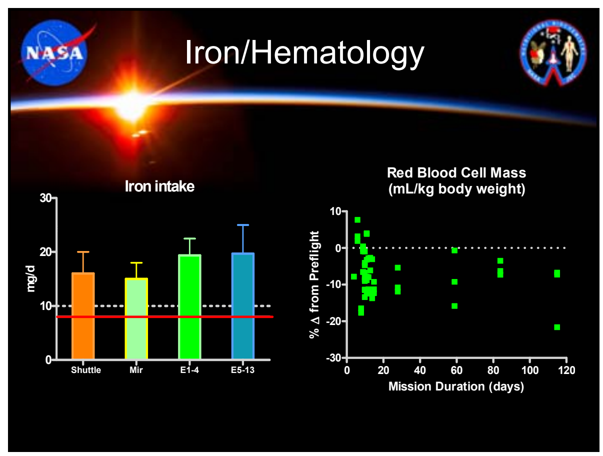
H+ release contributes to acid load

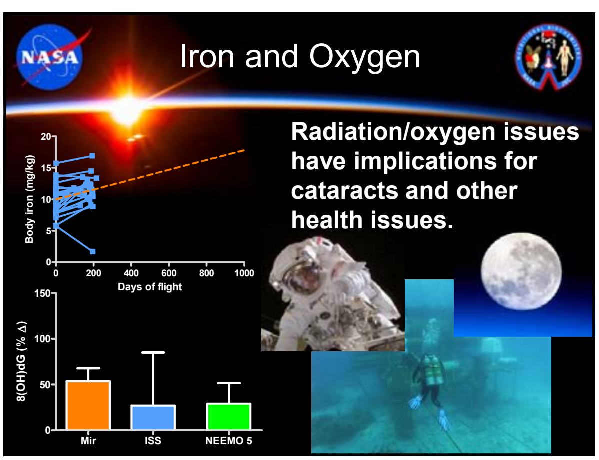


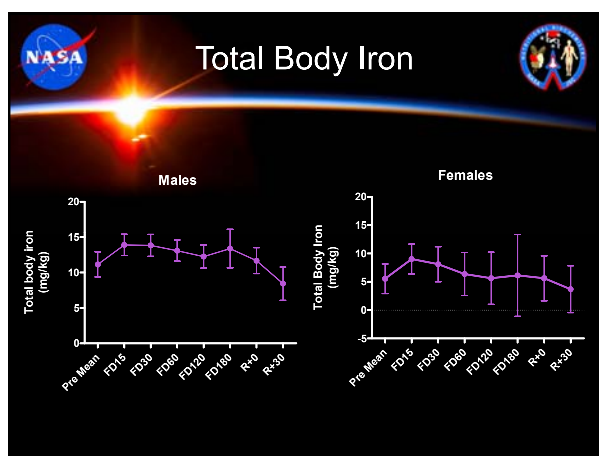

Acidosis
Nutritional Biochemistry Laboratory
SK/S.M. Smith
Feb 23, 2010
Recap 3
the higher the acid load and the older you are, the worse your kidney function is and the higher the body's acid level is maintained
'trade-offs' for maintaining acid-base balance include bone dissolution to provide base and muscle breakdown to increase renal H+ excretion
typical westernized diets are high in acid precursors
ameliorating the diet acid load, either with alkali supplements or by increased dietary alkali intake, is associated with higher bone mineral density, higher lean body mass, and
possibly improves vascular reactivity, at rest & with exercise
Pathophysiologic effects of acidosis
Metabolic acidosis in otherwise normal humans changes hormonal levels or responses to hormones
Hormone
Acidosis-induced response
Growth hormone (GH)
Suppressed GH secretion
Lower IGF-1 response
Insulin
Suppressed insulin-stimulated glucose metabolism
Insulin-like growth factor (IGF)-1
Decreased IGF-1 in plasma, and kidney and liver (but not in muscle)
Thyroid hormone
Glucocorticoids
Increased glucocorticoid production
Parathyroid hormone (PTH)
Decreased sensitivity of PTH secretion to changes in plasma calcium
Vitamin D
From Dr. L Frassetto (UCSF) 10/6/09 JSC presentation

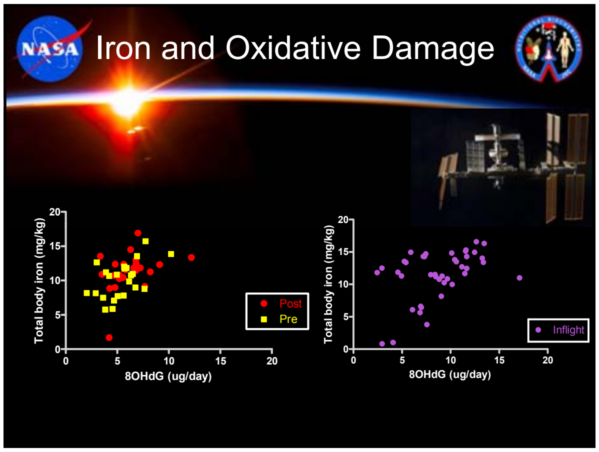

Acid/Base and Bone
Na+/H+ exchange in skin GAGs
Excess dietary sodium
CO3 2- Ca2+ CO3 2- Ca2+
Ca2+ excretion
H+ GAG- Na+
H+ GAG- Na+

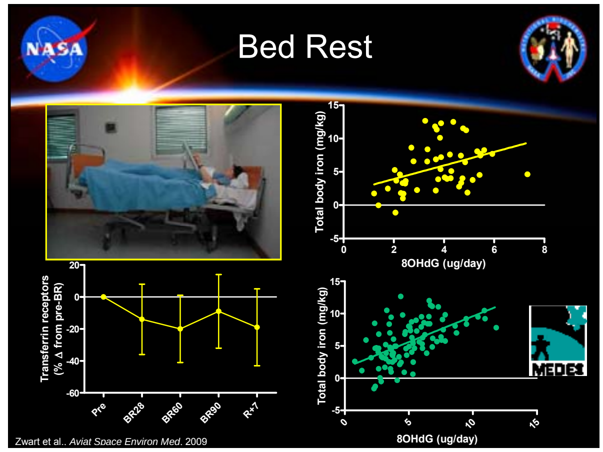

Iron (RBCs, and oxidative damage)

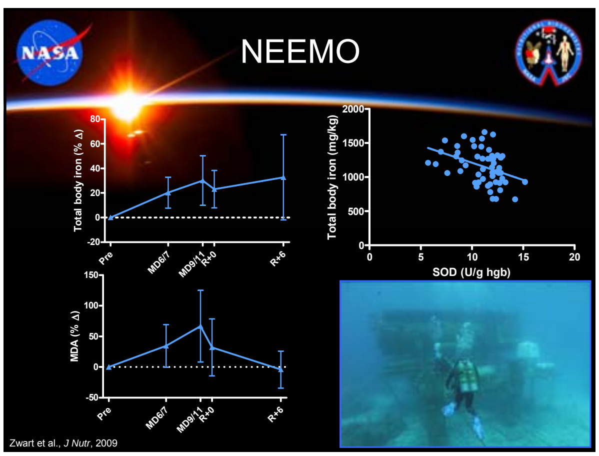

Iron/Hematology
Iron intake
mg/d
Shuttle
Mir
E1-4
E5-13
Red Blood Cell Mass (mL/kg body weight)
% Δ from Preflight
Mission Duration (days)

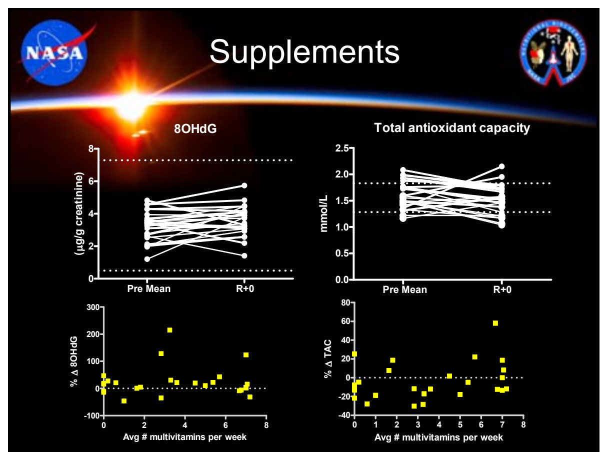

Iron and Oxygen
Body iron (mg/kg)
Days of flight
8(OH)dG (% Δ)
Mir
ISS
NEEMO 5
Radiation/oxygen issues have implications for cataracts and other health issues.

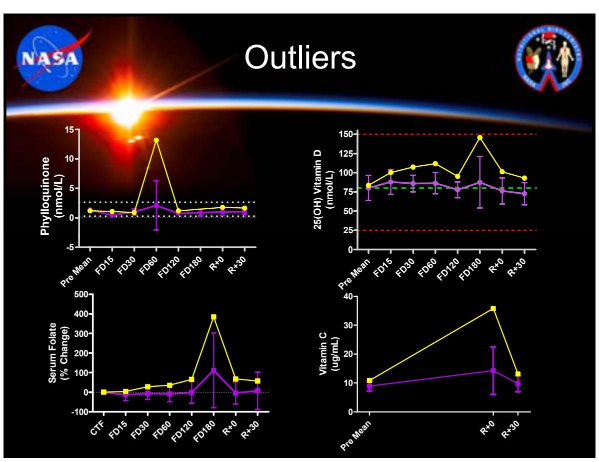

Total Body Iron
Males
Females
Total body iron (mg/kg)
Total Body Iron (mg/kg)
Pre Mean
FD15
FD30
FD60
FD120
FD180
R+0
R+30

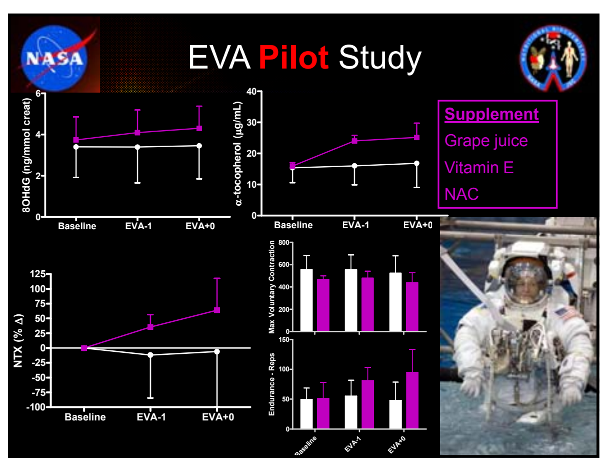

Iron and Oxidative Damage
Total body iron (mg/kg)
8OHdG (ug/day)
Post
Pre
Total body iron (mg/kg)
8OHdG (ug/day)
Inflight

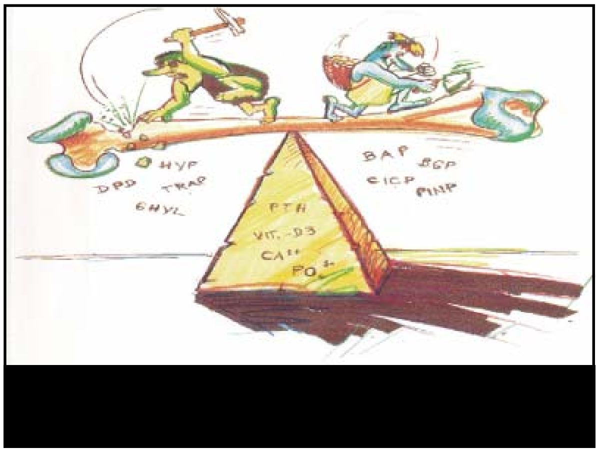

Bed Rest
Total body iron (mg/kg)
8OHdG (ug/day)
Transferrin receptors (% Δ from pre-BR)
Pre
BR28
BR60
BR90
R+7
Total body iron (mg/kg)
8OHdG (ug/day)
MEDES
Zwart et al., Aviat Space Environ Med, 2009

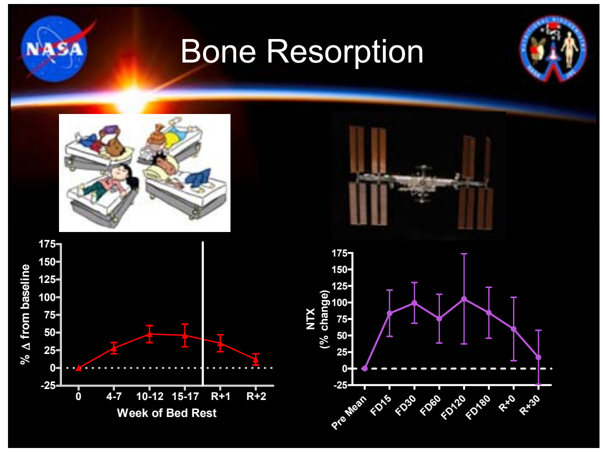

NEEMO
Total body iron (% Δ)
Pre
MD6/7
MD9/11
R+0
R+6
Total body iron (mg/kg)
SOD (U/g hgb)
MDA (% Δ)
Pre
MD6/7
MD9/11
R+0
R+6
Zwart et al., J Nutr, 2009

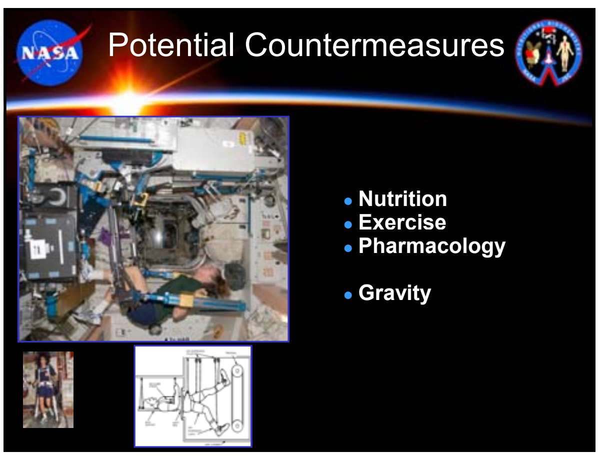

Supplements
8OHdG
(µg/g creatinine)
Pre Mean
R+0
Total antioxidant capacity
mmol/L
Pre Mean
R+0
% Δ 8OHdG
Avg # multivitamins per week
% Δ TAC
Avg # multivitamins per week

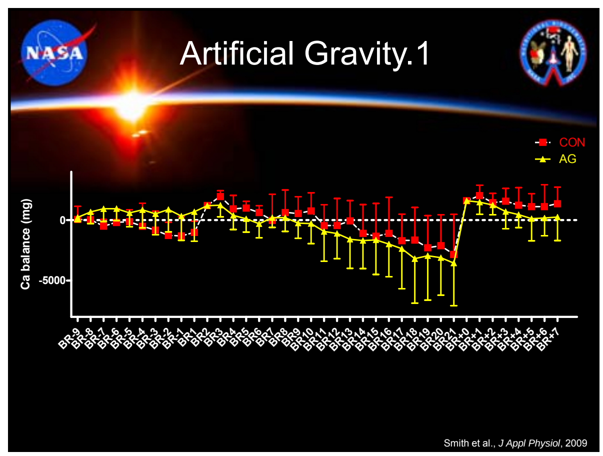

Outliers
Phylloquinone (nmol/L)
Pre Mean
FD15
FD30
FD60
FD120
FD180
R+0
R+30
25(OH) Vitamin D (nmol/L)
Pre Mean
FD15
FD30
FD60
FD120
FD180
R+0
R+30
Serum Folate (% Change)
CTF
FD15
FD30
FD60
FD120
FD180
R+0
R+30
Vitamin C (ug/mL)
Pre Mean
R+0
R+30

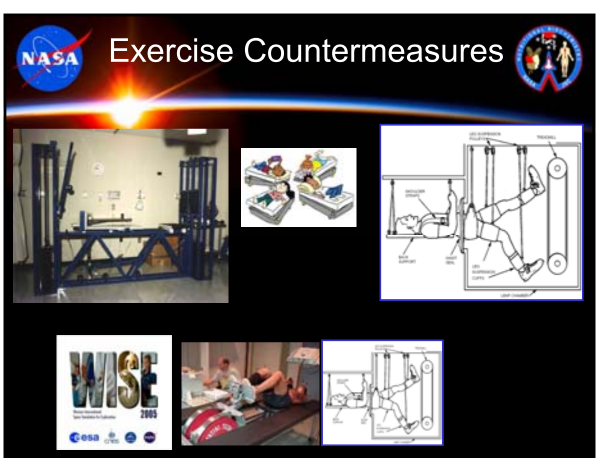

EVA Pilot Study
8OHdG (ng/mmol creat)
Baseline
EVA-1
EVA+0
α-tocopherol (µg/mL)
Baseline
EVA-1
EVA+0
Supplement
Grape juice
Vitamin E
NAC
NTX (% Δ)
Baseline
EVA-1
EVA+0
Max Voluntary Contraction
Endurance - Reps
Baseline
EVA-1
EVA+0

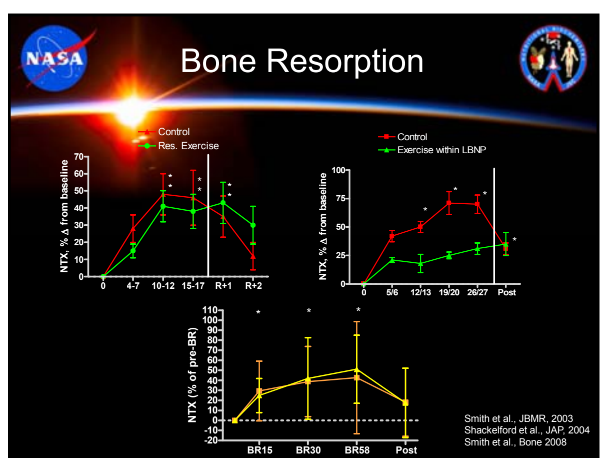


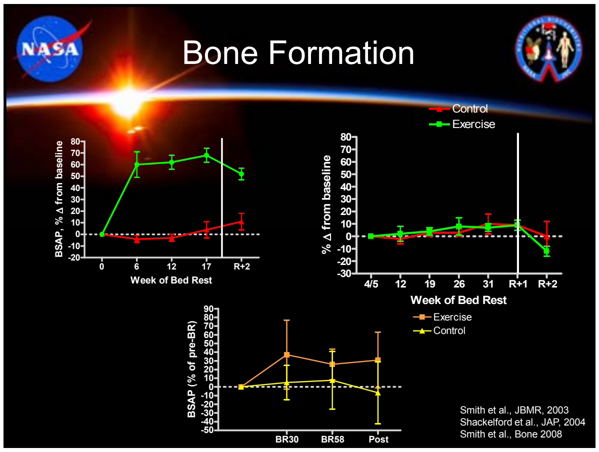

Bone Resorption
% Δ from baseline
Week of Bed Rest
0
4-7
10-12
15-17
R+1
R+2
NTX (% change)
Pre Mean
FD15
FD30
FD60
FD120
FD180
R+0
R+30

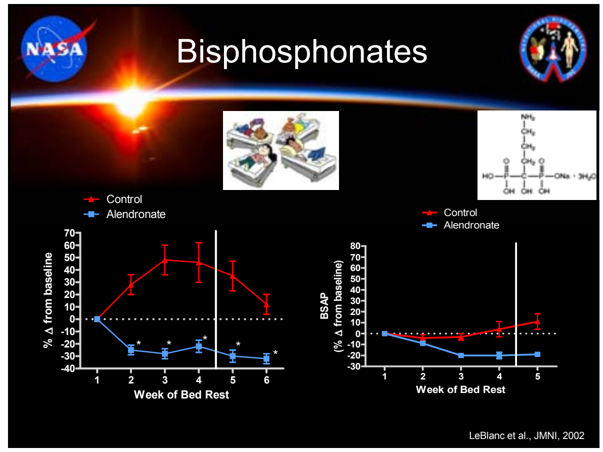

Potential Countermeasures
• Nutrition
• Exercise
• Pharmacology
• Gravity

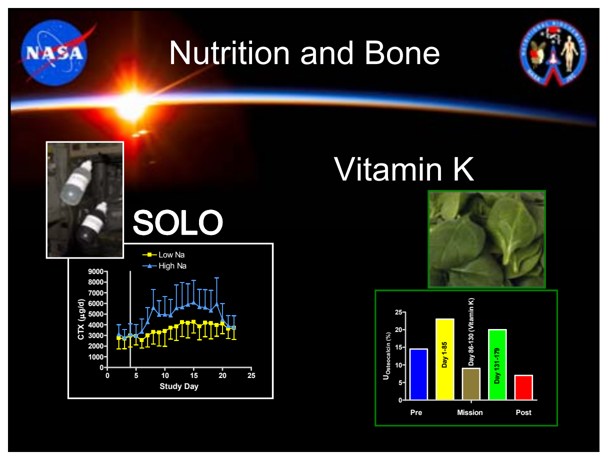

Artificial Gravity.1
CON
AG
Ca balance (mg)
Smith et al., J Appl Physiol, 2009


Exercise Countermeasures
WISE
2005


Bone Resorption
Control
Res. Exercise
NTX, % Δ from baseline
Control
Exercise within LBNP
NTX (% of pre-BR)
BR15
BR30
BR58
Post
Smith et al., JBMR, 2003
Shackelford et al., JAP, 2004
Smith et al., Bone 2008







Dietary Protein

Dietary protein increases urinary calcium

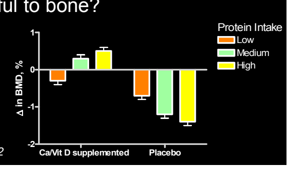
Oxidation of excess protein yields acid (H^+, H_2SO_4)

- Renal buffering
- Bone: reservoir of base

Osteoclasts are more active at lower pH

Excess protein: beneficial or harmful to bone?

- Many factors influence the net effect



Dawson-Hughes et al. 2002

Animal vs. Vegetable

Animal protein

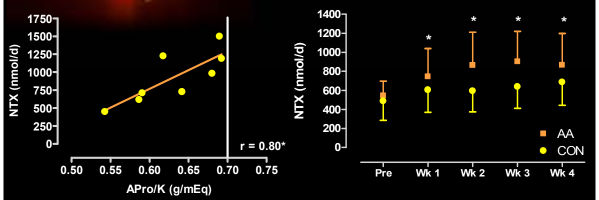
- Diets rich in animal protein tend to have greater overall acid potential
- Renal net acid excretion

Vegetables/fruits

- Also contain substantial amounts of base precursors (and K)

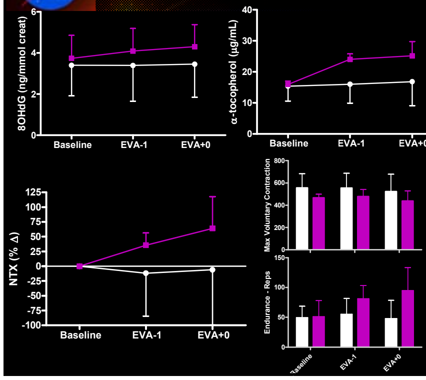
APro/K provides an estimation of acid/alkali load

APro:K and Bone



Zwart et al., *AJCN*, 2004
Zwart et al., J Appl Physiol, 2005

EVA Pilot Study



Supplement
Grape juice
Vitamin E
NAC

Pro K

Controlled dietary intake
High or Low APro:K
Monitored dietary intake

Blood/Urine markers

Design

Preflight
L-180: 4-d High APro:K
L-45: 4-d Low APro:K

Inflight
FD15: 4-d Low APro:K
FD30: 4-d Monitored Diet
FD60: 4-d Low APro:K
FD120: 4-d High APro:K
FD180: 4-d High APro:K

Postflight
R+30: 4-d Monitored Diet
R+180: 4-d Monitored Diet
R+365: 4-d Monitored Diet

NOTE: the low ratio diet is **NOT** low protein, and **NOT** vegetarian
NOTE: the pattern above (red or blue) is an example, your pattern may vary

Blood/Urine (24-h F; 48-h G) will be collected at the end of each session, and on L-10 and R+0

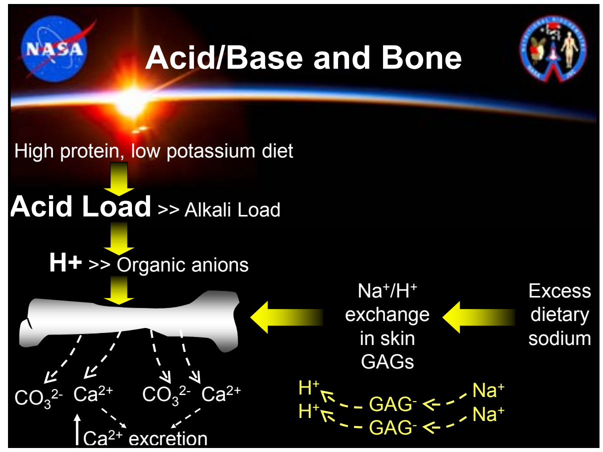
EXAMPLE Menu

High Apro/K Day 1 Example			
Oatmeal w/ Brown Sugar	Hot and Sour Soup		
Seasoned Scrambled Eggs	Grilled Pork Chop	Smoked Turkey	Bread Pudding
Granola Bar	Cheese Grits	Pasta w/Pesto Sauce	Butter Cookies
Fruit Cocktail	Green Beans & Mushrooms	Broccoli au Gratin	Almonds
Apple Cider	Cashews	Peanuts	Pineapple Drink
Tea	Brownies	Banana Pudding	
	Tropical Punch	Orange-Grapefruit Drink	

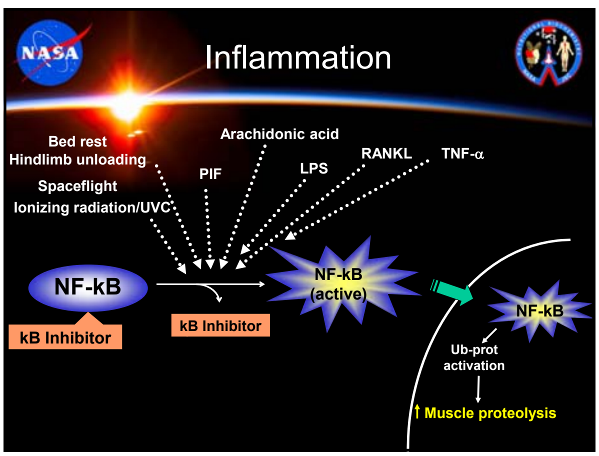
Low Apro/K Day 1 Example			
Oatmeal w/ Raisins & Spice	Vegetarian Vegetable Soup	Chicken Noodle Soup	
Waffles	Grilled Chicken	Tuna	Peanut Butter
Almonds	Cheese Tortellini	Curry Sauce w/ Vegetables	Tortillas
Cocoa	Carrot Coins	Creamed Spinach	Macadamia Nuts
Orange Juice	Tofu w/ Hot Mustard Sauce	Apples w/ Spice	Water (250 mL)
Tea	Potato Medley	Candy Coated Almonds	
	Candied Yams	Water (250 mL)	
	Japanese Tomato Jelly Drink		

Nutrition and Bone

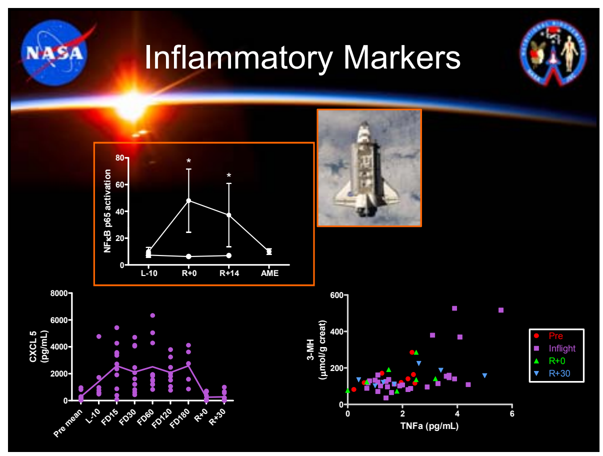
Pro K



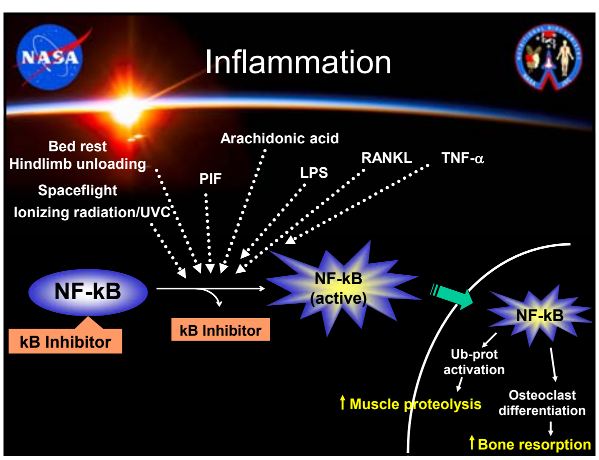
Acid/Base and Bone
High protein, low potassium diet
Acid Load >> Alkali Load
H+ >> Organic anions
Na+/H+ exchange in skin GAGs
Excess dietary sodium
CO3 2- Ca2+ CO3 2- Ca2+
Ca2+ excretion
H+ GAG- Na+
H+ GAG- Na+



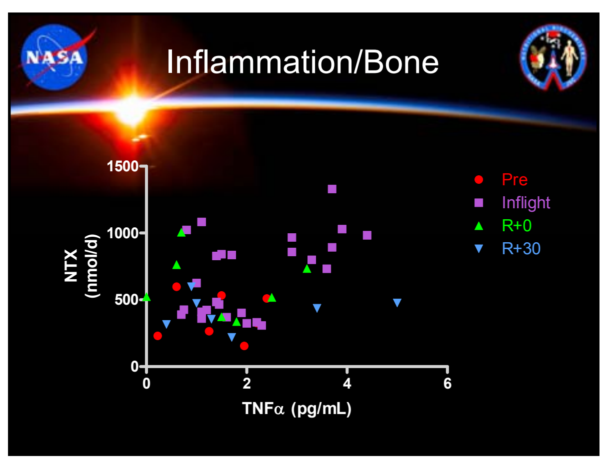
Inflammation
Bed rest
Hindlimb unloading
Spaceflight
Ionizing radiation/UVC
Arachidonic acid
PIF
LPS
RANKL
TNF-α
NF-kB
kB Inhibitor
kB Inhibitor
NF-kB (active)
NF-kB
Ub-prot activation
Muscle proteolysis



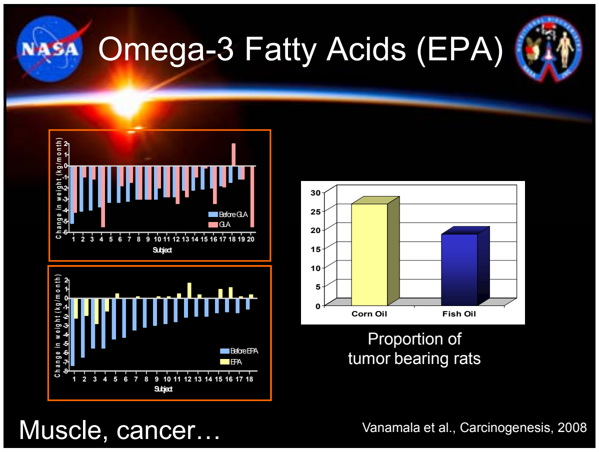
Inflammatory Markers
NFkB p65 activation
L-10 R+0 R+14 AME
CXCL 5 (pg/mL)
Pre mean L-10 FD15 FD30 FD60 FD120 FD180 R+0 R+30
3-MH (µmol/g creat)
TNFa (pg/mL)
Pre
Inflight
R+0
R+30

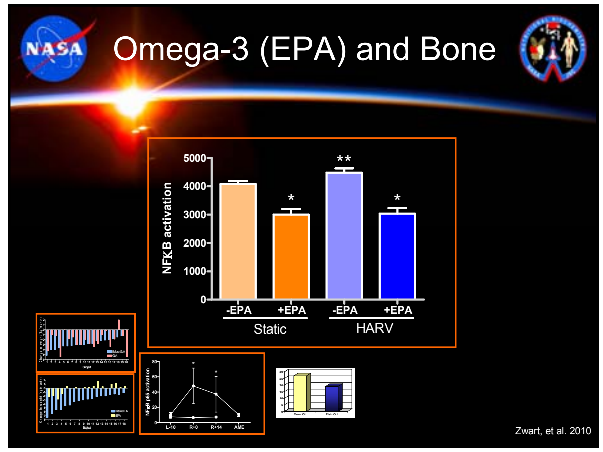


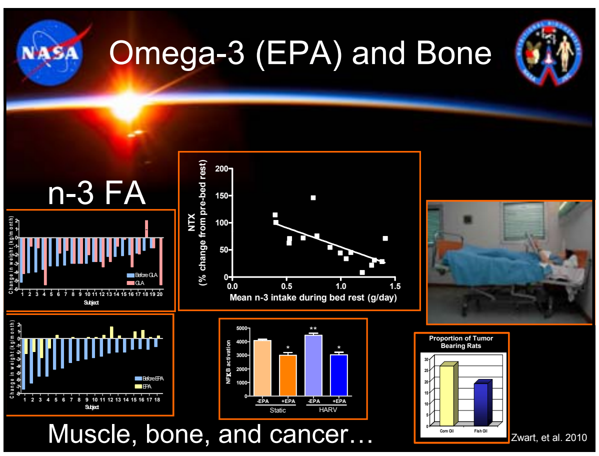
Inflammation
Bed rest
Hindlimb unloading
Spaceflight
Ionizing radiation/UVC
Arachidonic acid
PIF
LPS
RANKL
TNF-α
NF-kB
kB Inhibitor
kB Inhibitor
NF-kB (active)
NF-kB
Ub-prot activation
Muscle proteolysis
Osteoclast differentiation
Bone resorption

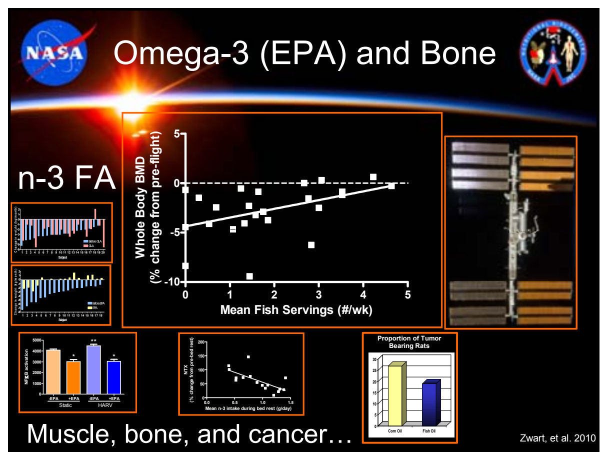


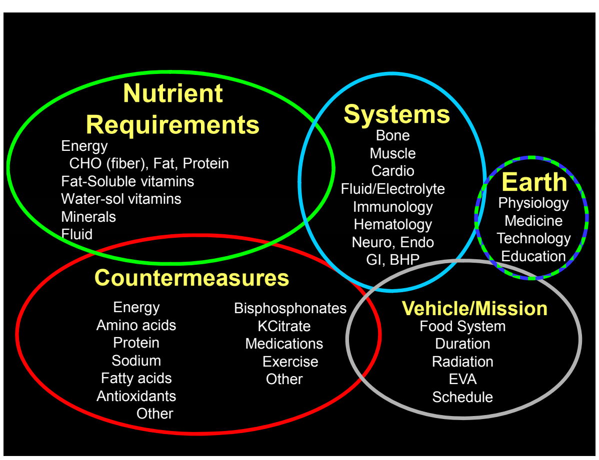
Inflammation/Bone
NTX (nmol/d)
1500
1000
500
0
0 2 4 6
TNFα (pg/mL)
Pre
Inflight
R+0
R+30


Omega-3 Fatty Acids (EPA)
Proportion of
tumor bearing rats
Corn Oil
Fish Oil
Muscle, cancer…
Vanamala et al., Carcinogenesis, 2008


Omega-3 (EPA) and Bone
NFKB activation
-EPA
+EPA
-EPA
+EPA
Static
HARV
Zwart, et al. 2010


Omega-3 (EPA) and Bone
n-3 FA
NTX
(% change from pre-bed rest)
Mean n-3 intake during bed rest (g/day)
Muscle, bone, and cancer…
Zwart, et al. 2010


Omega-3 (EPA) and Bone
n-3 FA
Whole Body BMD
(% change from pre-flight)
Mean Fish Servings (#/wk)
Muscle, bone, and cancer…
Zwart, et al. 2010


Nutrient
Requirements
Energy
CHO (fiber), Fat, Protein
Fat-Soluble vitamins
Water-sol vitamins
Minerals
Fluid
Systems
Bone
Muscle
Cardio
Fluid/Electrolyte
Immunology
Hematology
Neuro, Endo
GI, BHP
Earth
Physiology
Medicine
Technology
Education
Countermeasures
Energy
Amino acids
Protein
Sodium
Fatty acids
Antioxidants
Other
Bisphosphonates
KCitrate
Medications
Exercise
Other
Vehicle/Mission
Food System
Duration
Radiation
EVA
Schedule